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PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

Translation

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>09635</b>		Date of mailing (day/month/year)	
FOR FURTHER ACTION See paragraph 2 below			
International application No. <b>PCT/JP2004/005456</b>	International filing date (day/month/year) <b>16.04.2004</b>	Priority date (day/month/year) <b>18.04.2003</b>	
International Patent Classification (IPC) or both national classification and IPC			
Applicant <b>SENJU PHARMACEUTICAL CO. LTD.</b>			

1. This opinion contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the opinion
<input type="checkbox"/>	Box No. II	Priority
<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I

Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language  
\_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 13-16

because:

☒ the said international application, or the said claims Nos. 13-16  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matter of claims 13-16 relates to a method for treatment of the human body by therapy.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported  
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 13-16

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	1-12	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-12	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO
2. Citations and explanations:			
<p><u>Claims 1-12</u></p> <p>Document 1: M. NEGISHI et al., Seikagaku, 2002; 74 (5), 395-8, [Japanese]  Document 2: M. NIKOLIC, Int. J. Biochem Cell Biol, 2002, 34(7): 731-45  Document 3: M. LEHMANN et al., J. Neurosci., 1999, 19(17), 7537-47  Document 4: P. DERGHAM et al., J Neurosci, 2002, 22(15), 6570-7  Document 5: US 2002/0119140 A1  Document 6: WO 02/083175 A1 &amp; EP 1378247 A1  Document 7: WO 01/068607 A1 &amp; EP 1270570 A1  Document 8: JP 2003-073357 A</p> <p>As described in documents 1-8, the fact that the formation and expansion of neurite outgrowth is facilitated by inhibition of Rho is confirmed in a plural type of neurons. As a result, studying the effect for corneal nerves using a Rho inhibitor can be easily carried out by a person skilled in the art based on the knowledge obtained from these documents. Making use of the effect that the corneal nerves have on a variety of different diseases could easily be foreseen by a person skilled in the art.</p>			

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The subject matter of claims 1-12 relates to an agent for promoting corneal neural outgrowth formation, an agent for promoting extension of corneal neural axons, an agent for repairing corneal perception and a dry eye therapeutic agent whose active ingredient is a compound defined by the desired characteristics as a "Rho protein inhibitor." The subject matter of claims 1-12 encompasses all compounds which have these properties. However, what is disclosed in the sense of PCT Article 5 is merely an extremely small part of the compound claimed and is not fully supported by the disclosure of the specification in the sense of PCT Article 6.

Furthermore, even after taking into consideration the common general technical knowledge at the time of filing, the "Rho protein inhibitor" cannot specify the scope of the compounds which have these properties; therefore, claims 1-12 lack the requisite clarity of PCT Article 6.